Remarks

The September 21, 2004 Official Action has been carefully reviewed. In view of the amendments submitted herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset it is noted that a shortened statutory response period of three (3) months was set forth in the September 21, 2004 Official Action. Therefore, the initial due date for response was December 21, 2004. A petition for a 2 month extension of the response period is presented with this response, which is being filed within the two month extension period as February 21, 1005 fell on a federal holiday.

At page 4 of the Official Action, the Examiner has rejected claims 54-76 under 35 U.S.C. §112, second paragraph, as allegedly indefiniteness in several respects, of which are summarized at Page 17 of the September 21st Official Action.

The Examiner has also rejected claims 54-63, 64, 67, and 69-75 as allegedly failing to satisfy the written description requirement under 35 U.S.C. §112, first paragraph, for various reasons, which are also summarized at page 17 of the September 21st Official Action.

Lastly, the Examiner has rejected claim 76 under 35 U.S.C. §103(a) as allegedly unpatentable over Kuhstoss et al. (Gene (1996) 183:231-236) in view of U.S. Patent 5,672,491.

The foregoing rejections constitute all of the grounds set forth in the September 21, 2004 Official Action for refusing the present application.

In accordance with this amendment, claims 67, 69, 72, 74, and 76 have been cancelled. All of the rejections outstanding with respect to these claims are, therefore, rendered moot. The cancellation of claims 67, 69, 72, 74, and 76 should not be construed as indicative of Applicants' concurrence or acquiescence in the various rejections of claims 67, 69, 72, 74, and 76 as set forth in the September

21, 2004 Official Action, or otherwise as an abandonment of Applicants' efforts to secure patent protection on the subject matter of claims 67, 69, 72, 74, and 76. To the contrary, Applicants vigorously dispute those grounds of rejection. Such arguments as Applicants have to advance in rebuttal, however, are being reserved for a continuing application, which is expected to be filed and include claims directed to the subject matter of cancelled claims 67, 69, 72, 74, and 76.

Claims 54, 60, 63, 64, 70, 71, 73, and 75 have been amended in accordance with this amendment. The amendments to claim 73 and 75 are believed to eliminate what the Examiner characterizes as "inherent functionality". Claims 54 and 64 have been amended to eliminate language perceived by the Examiner to be indefinite. Claim 54 has also been amended to state the meaning of the term "engineered KSq domain." Support for his amendment can be found at page 18, lines 12-20 and at page 27, lines 16-21. Claim 63 has been amended to more clearly define the claimed subject matter. Support for this amendment can be found, for example, at page 27, lines 3-15. Claims 60, 64, 70, and 71 have been amended to remove language which the Examiner perceives as introducing new matter. Claim 70 has also been amended to include the claim language of claim 64, from which it previously depended.

No new matter has been introduced into this application by reason of any of the amendments presented herewith.

CLAIMS 54-76, AS AMENDED, MEET THE REQUIREMENTS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

The Examiner has rejected claims 54-76 under 35 U.S.C. §112, second paragraph as allegedly indefinite for the reasons set forth below.

Claims 54-76 stand rejected because the phrase "at least the first of said extension modules is not naturally associated with said loading module," which is recited in all

of the independent claims (i.e., claims 54, 64, and 72-76) is deemed to be unclear. The Examiner asserts that it is unclear which part of the loading domain needs to be "not naturally associated" with the at least first extension module.

Applicants continue to take exception to the Examiner's position. However, in an effort to eliminate any ambiguity, Applicants have deleted the allegedly indefinite phrase from claim 54. Claim 54, as currently amended, specifically recites that the engineered-KSq domain of the loading module is obtained by replacing the active site cysteine of a KS domain from an extension module with a glutamine. Inasmuch as the engineered-KSq is synthetically generated, the engineered-KSq domain, and thus the entire loading module, cannot be "naturally associated" with any extension module.

Similarly, Applicants have also deleted the allegedly ambiguous phrase from claim 64 as being redundant. Amended claim 64 recites that the AT domain of the loading module is selected from the group consisting of AT domains from module 6 of the niddamycin PKS, module 4 of the FK506 PKS, and module 5 of the spiramycin PKS. Inasmuch as the recited AT domains are from extension modules and not any naturally occurring loading module, Applicants respectfully submit that it necessarily follows that the extension modules of the instantly claimed PKS are not "naturally associated" with either the AT domain of the loading module or the loading module as a whole.

Furthermore, claims 73 and 75 specifically recite full loading modules from a specific PKS. Accordingly, Applicants submit that if an extension module is not "naturally associated" with one of the domains of the recited loading module, then the extension module a fortiori cannot be "naturally associated" with any other domain of the loading module or the loading module as a whole. Accordingly, the Examiner's contention that these claims are allegedly

ambiguous as to "what the extension modules must not be naturally associated with" has been fully refuted.

As already noted claims 72, 74, and 76 have been cancelled.

In light of the foregoing, any indefiniteness or lack of clarity that may have been engendered by the previous wording of claims 54-76, insofar as the nature of the loading modular is concerned, has now been eliminated.

Second, the Examiner contends that the phrase "wherein the starter unit is derived from a loading domain," recited in claim 63, is unclear. In order to eliminate any possible ambiguity, Applicants have replaced the allegedly indefinite phrase with the recitation that the starter unit is derived by the **action** of the engineered-KSq domain on the enzyme-bound product of the AT domain of the loading module. Support for this amendment can be found at page 27, lines 3-15.

Lastly, claims 73-76 have been rejected because it is the Examiner's position that the inclusion of the inherent functional language is confusing. Applicants have, in an effort to more clearly recite the claimed subject matter, deleted parts a) and b) from claims 73 and 75, thereby removing the inherent functional language from those claims. Applicants note that claims 74 and 76 have been cancelled, thereby rendering moot this rejection as to those claims.

In light of all of the foregoing, Applicants submit that the rejections of claims 54-76 under 35 U.S.C. §112, second paragraph for alleged indefiniteness are untenable and request their withdrawal.

CLAIMS 54-63, 64, 67, AND 69-75, AS AMENDED, SATISFY THE WRITTEN DESCRIPTION REQUIREMENT UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The Examiner has rejected claims 54-63, 64, 67, and

69-75 as allegedly failing to satisfy the written description requirement under 35 U.S.C. §112, first paragraph, for the reasons set forth below.

First, the Examiner has maintained the rejection of claims 54-63 because the specification allegedly fails to provide adequate written description for hybrid polyketide synthases comprising engineered KSq domains. Applicants disagree with the Examiner for the reasons already of record. However, in the interest of expediting prosecution, Applicants have amended independent claim 54, from which claims 55-63 depend, to recite that the engineered KSq domain is obtained by replacing the active site cysteine of a KS domain from an extension module to a glutamine residue. Support for this amendment can be found, for example, at page 18, lines 12-20 and at page 27, lines 16-21. Applicants submit that a skilled artisan, upon consideration of the instant specification as of the priority date of the instant application, would clearly have conclude that applicants had the wherewithal to generate KSq domains from KS domains of extension modules by replacing the active site cysteine with glutamine by, for example, site-directed mutagenesis. Accordingly, it is evident that a skilled artisan would understand or appreciate that Applicants were in possession of the instantly claimed invention.

Second, the Examiner has rejected claims 64, 67, and 71 for allegedly containing new matter. It is the Examiner's position that while the specification provides support for a loading module comprising a KSq domain from the oleandomycin PKS, an AT2 domain from the rapamycin PKS, and an ACP domain from the DEBS loading module, the specification allegedly does not adequately provide support for a loading module comprising the AT2 domain from the rapamycin PKS, any KSq domain, and any ACP domain. Applicants do not agree with the Examiner's assessment of the specification in this regard. Nevertheless, in the interest of expediting the prosecution of the instant application, Applicants have amended claim 64 to remove

reference to the AT2 domain from the rapamycin PKS, and claim 67 has been cancelled. Inasmuch as claim 71 depends from claim 64 and does not recite the AT2 domain from the rapamycin PKS, Applicants submit the instant rejection has been overcome.

Third, claims 70 and 72 have also been rejected for allegedly containing new matter. The Examiner contends that while the specification provides support for a loading module comprising a KSq domain from the oleandomycin PKS, an AT2 domain from the rapamycin PKS, and an ACP domain from the DEBS loading module, the specification allegedly does not adequately provide support for any loading module comprising the KSq domain from the oleandomycin PKS. Again, Applicants disagree with the Examiner, but have nonetheless amended claim 70 to recite the exemplified loading module and have cancelled claim 72. These amendments are presented in order to expedite prosecution of the instant application. Support for the amendment to claim 70 can be found, for example, at page 47, lines 4-12.

Fourth, the Examiner has rejected claim 75 for allegedly containing new matter. Specifically, the Examiner contends that the specification does not provide support for a hybrid PKS having a tylosin loading module and a plurality of extension modules which produces a 12- or 14-membered macrolide. Applicants respectfully disagree. At page 21, line 16 through page 22, line 7, the instant specification discloses that:

> "It is similarly useful to provide a loading module of the type KSq-ATq-ACP for a PKS gene assembly which produces a 12-, 14-**or** 16-membered macrolide in order to prepare a 12-, 14-**or** 16-membered macrolide... Particularly suitable PKSs for this purpose are the components of PKSs for the biosynthesis of ... tylosin... A particularly suitable source of the genes encoding a loading module of the type KSq-ATq-ACP is the **loading module of tylosin** which is specific for the loading of methylmalonate units which are decarboxylated to propionate starter units." [Emphasis added.]

It is readily apparent that the above passage teaches that 12-membered, 14-membered, **or** 16-memebered macrolides may be produced with a PKS comprising the loading module of tylosin. Inasmuch as the above passage teaches that any of 3 macrolides of differing member size may be produced, Applicants submit that the specification provides adequate support for a claim drawn to hybrid polyketide synthase comprising a tylosin loading module which produces either 12-membered macrolides or 14-memebred macrolides.

Fifth, the Examiner has also rejected claims 60, 64, and 69-71 because the prior art allegedly does not teach the PKS gene cluster for monensin. Thus, the Examiner concludes that while the concept of the AT domain of module 5 of the monensin polyketide synthase is set forth in the instant application, the specification fails to provide adequate support by failing to provide a representative species. Applicants here again do not concur with the Examiner's position; however, in an effort to expedite prosecution of the instant application, Applicants have removed reference to the AT domain of module 5 of the monensin polyketide synthase from claims 60 and 64 and cancelled claims 69. Notably, claims 70 and 71 do not refer to the AT domain of module 5 of the monensin polyketide synthase.

Sixth, it is also the Examiner's position that the specification fails to provide adequate support for the oleandomycin loading module or the KSq domain thereof, as recited in claims 70, 72, and 74. Applicants respectfully disagree with the Examiner. At page 30, lines 17-21 and Figure 4, the instant specification provides the amino acid sequence of the KSq-AT didomain of the oleandomycin PKS loading module. Applicants also submit that the skilled artisan would be well aware of the boundaries between the KSq and ATq domains based on the sequence alignment with other well-known didomains. Furthermore, the instant specification,

at page 49, lines 17-18, provides specific PCR primers for the amplification of the DNA encoding the KSq domain of the oleandomycin PKS. Notably, claim 70 is drawn to a protein, namely a polyketide synthase, and therefore the disclosure of the amino acid sequence of the KSq domain of the oleandomycin loading module provides adequate support for the instantly claimed invention. Accordingly, Applicants submit that the "KSq domain of the oleandomycin loading module," as recited in claim 70, is clearly and fully supported by the specification.

It is also the Applicants' position that a skilled artisan, upon reviewing the present specification would readily appreciate that Applicants were in possession of the means to isolate the entire oleandomycin loading module based on the disclosure of the amino acid sequence of the didomain and the described PCR primers. However, in the interest of expediting prosecution of the instant application, Applicants have cancelled claim 74 which recited the entire oleandomycin loading module. Also, claim 72 is cancelled for reasons set forth hereinabove.

Seventh, the Examiner has rejected claim 71 because the specification allegedly fails to provide adequate written support for extension modules from the immunomycin PKS. While not agreeing with the Examiner, Applicants have amended claim 71 to remove reference to these extension modules.

Lastly, the Examiner has rejected claim 73 because the specification allegedly fails to provide adequate support for the recited monensin loading module. Applicants respectfully disagree with the Examiner.

The Guidelines for Examination of Patent Applications under the 35 U.S.C. §112, P 1, "Written Description" Requirement (Guidelines), states that:

> "Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached considering a number of factors. Factors to be considered in determining whether there is

> sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention." 66 Fed. Reg. 1099 (Jan. 5, 2001), at 1106.

Furthermore, the U.S. Court of Appeals for the Federal Circuit has stated that the written description requirement can be met by:

> "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some other combination of such characteristics." In re Wallach, 378 F.3d 1330 (Fed Cir. 2004).

Notably, in In re Wallach, Appellants disclosed in their patent application a partial amino acid sequence that was about 5% of the total amino acid sequence of the TBP-II protein. Id. at 1334. The Appellants also indicated that the TBP-II protein was about 30 kDa, present in human urine, and was capable of selectively inhibiting the cytotoxic effect of tumor necrosis factor. Id. at 1331. While In re Wallach deals with a patent application claiming DNA molecules encoding TBP-II, Applicants note that the disclosure of the partial amino acid sequence and the other characteristics of TBP-II was sufficient "to satisfy the PTO that they were in possession of the claimed" TBP-II protein in a divisional application. Id. at 1334.

Applicants respectfully submit that the instant specification provides substantially more identifying characteristics for the purposes of satisfying the written description requirement of 35 U.S.C. §112, first paragraph, than a partial amino acid sequence of only 5% of the total protein, as was the case in In re Wallach. In Figure 4 of the instant specification, the amino acid sequence of the KSq and

AT domains of the monensin loading module is provided. Inasmuch as the loading module comprises three domains, namely KSq-AT-ACP, Applicants have provided the amino acid sequence of 2 of the 3 domains of the claimed monensin loading module. Furthermore, by identifying the remaining third domain as an ACP domain, Applicants have also identified the function of this domain, namely an acyl carrier protein. Additionally, Examples 1-3 (pages 32-35) of the instant specification provide specific primers for the amplification of the monensin loading module, creation of a nucleic acid molecule encoding a hybrid PKS comprising the monensin loading module with erythromycin extension modules, expression of the hybrid PKS, and production of a polyketide from the hybrid PKS comprising the monensin loading module.

Thus, the instant specification provides a substantial portion of the amino acid sequence, functional characteristics of the sequenced and non-sequenced domains, as well as a method of making the claimed monensin loading module and a hybrid PKS comprising the monensin loading module. Applicants respectfully submit that these characteristics, in light of the standards set forth in the Guidelines, clearly provide adequate disclosure to satisfy the written description requirement. Accordingly, Applicants respectfully submit that the instant rejection of claim 73 is improper.

For all of the foregoing reasons, Applicants submit that the rejections of claims 54-63, 64, 67, and 69-75 for allegedly failing to satisfy the written description requirement of 35 U.S.C. §112, first paragraph are untenable and request their withdrawal.

THE REJECTION OF CLAIM 76 AS ALLEGEDLY UNPATENTABLE OVER KUHSTOSS ET AL. IN VIEW OF U.S. PATENT 5,672,491 HAS BEEN RENDERED MOOT

The Examiner has rejected claim 76 under 35 U.S.C. §103(a) as allegedly unpatentable over Kuhstoss et al. (Gene

(1996) 183:231-236) in view of U.S. Patent 5,672,491. Kuhstoss et al. allegedly disclose a hybrid PKS comprising the loading module from the tylosin PKS and the extension modules from the spiramycin PKS. Kuhstoss et al. also allegedly teach that the spiramycin loading module comprises a KSq domain. The Examiner acknowledges that Kuhstoss et al. do not disclose a hydrid PKS comprising the loading module of the spiramycin PKS and the extension modules of the tylosin PKS. It is the Examiner's position, however, that it would have been obvious to a skilled artisan to make the "reverse" of the hybrid PKS disclosed in Kuhstoss et al. because of the teaching in the '491 patent that hybrid type I PKSs may comprise domains and modules from type I PKSs such as tylosin and spiromycin.

Applicants respectfully disagree with the Examiner. However, in the interest of expediting prosecution of the instant application, Applicants have cancelled claim 76. Accordingly, the Examiner's rejection of claim 76 as allegedly unpatentable over Kuhstoss et al. in view of U.S. Patent 5,672,491 has been rendered moot.

CONCLUSION

It is respectfully requested that the amendments presented herewith be entered in this application, since the amendments are primarily formal, rather than substantive in nature. This amendment is believed to clearly place the pending claims in condition for allowance. In any event, the claims as presently amended are believed to eliminate certain issues and better define other issues which would be raised on appeal, should an appeal be necessary in this case. These amendments were not presented earlier, because the arguments to which they respond, for the most part, were advanced for the first time in the September 21, 2004 Official Action.

In view of the amendments presented herewith and the foregoing remarks, it is respectfully urged that the rejections set forth in the September 21, 2004 Official Action

be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number give below.

Respectfully submitted,
DANN, DORFMAN, HERRELL AND SKILLMAN
A Professional Corporation

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Enclosure: In re Wallach, 378 F.3d 1330 (Fed. Cir. 2004)

LEXSEE 378 F.3D 1330

IN RE DAVID WALLACH, HARTMUT ENGELMANN, DAN ADERKA, DANIELA NOVICK, and MENACHEM RUBINSTEIN

03-1327

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

378 F.3d 1330; 2004 U.S. App. LEXIS 16546; 71 U.S.P.Q.2D (BNA) 1939

August 11, 2004, Decided

PRIOR HISTORY: [**1] Appealed from: United States Patent and Trademark Office Board of Patent Appeals and Interferences. (Serial No. 08/485,129). *Ex parte David Wallach, 2002 Pat. App. LEXIS 327 (Bd. Pat. App. & Interferences, Dec. 26, 2002)*

DISPOSITION: Affirmed.

LexisNexis(R) Headnotes

COUNSEL: Roger L. Browdy, Browdy and Neimark, P.L.L.C., of Washington, DC, argued for appellants.

Mary L. Kelly, Associate Solicitor, Office of the Solicitor, United States Patent and Trademark Office, of Arlington, Virginia, argued for the Director of the U.S. Patent and Trademark Office. With her on the brief were John M. Whealan, Solicitor; and Raymond T. Chen, Associate Solicitor. Of counsel were Stephen Walsh and William LaMarca, Associate Solicitors.

JUDGES: Before MAYER, Chief Judge, LOURIE and GAJARSA, Circuit Judges.

OPINIONBY: LOURIE

OPINION: [*1331] LOURIE, Circuit Judge.

David Wallach, Hartmut Engelmann, Dan Aderka, Daniela Novick, and Menachem Rubinstein (collectively, "Appellants") appeal from the decision of the United States Patent and Trademark Office ("PTO") Board of Patent Appeals and Interferences affirming the rejection of claims 11-13, 35-38, 43, 44, 46-49, 51-54, 56-61, 63, and 64 of United States patent application 08/485,129 under the written description requirement of *35 U.S.C. § 112. In re Wallach, 2002 Pat. App. LEXIS 327, Appeal No.* [**2] *2002-1363 (Bd. Pat. Apps. & Interfs. Dec. 26, 2002)*. We affirm.

BACKGROUND

In the 1980s, Appellants apparently discovered two specific proteins isolated from human urine that, among other things, selectively inhibit the cytotoxic effect of tumor necrosis factor ("TNF"). They named the compounds TNF binding proteins I & II ("TBP-I" and "TBP-II"). After obtaining a partial amino acid sequence of the N-terminal portion of TBP-II and determining that the complete protein has a molecular weight of about 30 kilodaltons ("kDa") when measured by sodium dodecyl sulfate polyacrylamide gel electrophoresis ("SDS-PAGE") under reducing conditions, Appellants filed a patent application including, inter alia, claims directed to proteins having that molecular weight and partial sequence (i.e., threonine-proline-tyrosine-alanine-proline-glutamic acid-proline-glycine-serine-threonine, or "Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr") and having the ability to inhibit the cytotoxic effect of TNF. Appellants' application also included [*1332] claims to isolated DNA molecules that encode the claimed proteins. The PTO issued a restriction requirement and Appellants filed divisional applications. The claims [**3] directed to the proteins having the stated partial sequence are currently involved in an interference proceeding and are not at issue here. The claims at issue, those directed to the DNA, were rejected under *§ 112* "as based on a specification which does not provide an adequate written description of the claimed invention." *Wallach, 2002 Pat. App. LEXIS 327 at *2*. After several unsuccessful attempts to traverse that rejection, Appellants appealed to the Board.

Citing this court's decisions in *Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (Fed. Cir. 1991), Fiers v. Revel, 984 F.2d 1164 (Fed. Cir. 1993)*, and *Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997)*, the Board affirmed the examiner's rejection. In particular, the Board held that "(1) applicants do not describe the genetic material sought to be patented in claim 11 with sufficient specificity in their specification; and (2) the examiner did not err in finding that claim 11 is based on a specification which does not provide adequate, written descriptive support for the claimed subject

matter." *Wallach, 2002 Pat. App. LEXIS 327 at *13.* n1

n1 The Board treated all of the appealed claims as standing or falling together with claim 11, pursuant to *37 C.F.R. § 1.192(c)(7)*, and decided the appeal on the basis of that claim alone. *Wallach, 2002 Pat. App. LEXIS 327 at *6.* Appellants do not challenge the Board on that point, and we likewise decide this appeal only on the basis of that claim.

[**4]

Appellants now appeal. We have jurisdiction pursuant to *28 U.S.C. § 1295(a)(4)(A).*

DISCUSSION

Claim 11 of the '129 application reads as follows:

> 11. An isolated DNA molecule comprising a contiguous nucleotide sequence coding for a protein consisting of naturally occurring human Tumor Necrosis Factor (TNF) Binding Protein II, herein designated TBP-II, said TBP-II including the amino acid sequence: Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr in the portion of the protein sequenced by N-terminal sequence analysis, said protein having the ability to inhibit the cytotoxic effect of TNF, wherein said naturally occurring TBP-II protein is the same as that protein having the ability to inhibit the cytotoxic effect of TNF which, after being purified by subjecting a crude protein recovered from a dialyzed concentrate of human urine to affinity chromatography on a column of immobilized TNF, elutes from a reversed-phase high pressure liquid chromatography column as a single peak in a fraction corresponding to about 31% acetonitrile and shows a molecular weight of about 30 kDa when measured by SDS-PAGE under reducing conditions.

On appeal, Appellants argue that the [**5] PTO has effectively conceded that the TBP-II protein, which the claimed isolated DNA encodes, is sufficiently described in the specification to comply with *§ 112*, because the claims of United States patent application 07/930,443, of which the '129 application is a division (which, by definition, has the same specification), have been allowed but for their involvement in an interference proceeding. According to Appellants, those claims do not differ in substance from the present claims except insofar as they are directed to a partial protein sequence, rather than to the DNA sequences encoding the protein. Appellants contend that that is not a meaningful distinction, because the genetic code is based on an unequivocal correspondence between amino acids and encoding DNA codons, and determination of the amino [*1333] acid sequence of a protein automatically puts one in possession of all DNA sequences encoding that protein. Appellants also argue that the complete amino acid sequence of a protein is an inherent property of an isolated protein that has been fully characterized by partial amino acid sequence and other characteristics, and that the complete amino acid sequence of a protein therefore [**6] puts one in possession of all DNA sequences encoding it. Therefore, according to Appellants, the specification establishes that the present inventors were in fact in possession of the entire claimed genus of DNA sequences at the time the application was filed.

Appellants also argue that this case is distinguishable from past written description cases such as Amgen v. Chugai and Fiers, because Appellants have provided an actual amino acid sequence that is encoded by the claimed DNA, not simply the name of the protein and a statement that the DNA can be obtained by reverse transcription. Appellants contend that this case is also distinguishable from Lilly because the inventors here are not attempting to claim DNA molecules encoding a plurality of unknown proteins from various species having no common features, but only those encoding the single protein sequence that is actually set forth in the specification. Finally, Appellants argue that, because there is a known correlation between the function (i.e., encoding a specified amino acid sequence) and structure, this is the quintessential example of the sort of functional description permitted by *§ 112* in view of our [**7] decision in *Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316 (Fed. Cir. 2002).* Appellants argue that our recent decision in *Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313 (Fed. Cir. 2003),* which issued after the Board's opinion in the present case, reaffirmed that *§ 112* only requires a court to determine whether a specification conveys to one of ordinary skill in the art as of the filing date that the inventors invented the claimed subject matter.

The PTO responds by arguing that Appellants' specification includes neither any actual DNA sequence within the scope of the claims nor the complete amino acid sequence of the TBP-II protein, but only the sequence of ten out of the 185-192 amino acids that make up the protein. Furthermore, the PTO argues, the only disclosed function of the claimed DNA molecules is to encode the TBP-II protein, and no information is provided from which the claimed DNA molecules can be distinguished from other DNA molecules. According to the PTO, the identity of the nucleic acid encoding a protein is not an inherent property of the protein. If Appellants' reasoning were accepted, the

PTO asserts, the result would [**8] be that the disclosure of an isolated protein would be prior art under *§ 102* with respect to claims directed to any nucleic acid encoding the protein. Finally, the PTO contends, substantial evidence supports the Board's factual finding that Appellants' specification does not adequately describe the claimed genus of DNA molecules.

As a preliminary matter, we agree with Appellants that the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it, and that one of ordinary skill in the art at the time the '129 application was filed may have therefore been in possession of the entire genus of DNA sequences that can encode the disclosed partial protein sequence, even if individual species within that genus might not have been described or rendered obvious. Cf. *In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995)*. Thus, for example, the RNA molecules required to encode the described amino acid sequence must necessarily have the following sequence: ACN-CCN-UAY-GCN-CCN-GAR-CCN-GGN-(UCN or AGY)-ACN, [*1334] where N is A, G, C, or U; Y is U or C; and R is G or A. See James D. Watson et al., [**9] Molecular Biology of the Gene 356-57 (3d ed. 1977), cited in '129 application. A claim to the genus of DNA molecules complementary to the RNA having the sequences encompassed by that formula, even if defined only in terms of the protein sequence that the DNA molecules encode, while containing a large number of species, is definite in scope and provides the public notice required of patent applicants. Indeed, the PTO's Manual of Patent Examining Procedure ("MPEP") states:

> Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species.

MPEP [**10] § 2163.II.A.3.a.ii. (8th ed., rev. 2 2001).

Moreover, we see no reason to require a patent applicant to list every possible permutation of the nucleic acid sequences that can encode a particular protein for which the amino acid sequence is disclosed, given the fact that it is, as explained above, a routine matter to convert back and forth between an amino acid sequence and the sequences of the nucleic acid molecules that can encode it.

Nonetheless, Appellants did not claim the nucleic acid molecules that encode the simple protein sequence that they disclosed. Rather, they claimed the nucleic acids encoding a protein for which they provided only a partial sequence. Appellants concede that it is now known that urinary TBP-II has a sequence of 185-192 amino acids. Without the approximately 95% of the amino acid sequence that Appellants did not disclose, we cannot say that the DNA molecules claimed in the '129 application have been described. As the MPEP explains, "disclosure of a partial structure without additional characterization of the product may not be sufficient to evidence possession of the claimed invention." MPEP § 2163.II.A.3.a.i. The Board's decision was thus consistent [**11] with its guidance in the MPEP. Here, Appellants disclosed a partial structure and possibly sufficient additional characterization of the TBP-II protein to satisfy the PTO that they were in possession of the claimed subject matter in their '443 application, but that additional characterization contributes little, if anything, to the description of the DNA molecules claimed in the '129 application.

Appellants argue that "as appellants have demonstrated possession of the TBP-II protein, appellants were also necessarily in possession of its inherent amino acid sequence, as well as all of the DNA sequences encoding that amino acid sequence." We disagree. Whether Appellants were in possession of the protein says nothing about whether they were in possession of the protein's amino acid sequence. Although Appellants correctly point out that a protein's amino acid sequence is an inherent property of the protein, the fact that Appellants may have isolated and thus physically possessed [*1335] TBP-II does not amount to knowledge of that protein's sequence or possession of any of its other descriptive properties. Appellants have not provided any evidence that the full amino acid sequence of a protein [**12] can be deduced from a partial sequence and the limited additional physical characteristics that they have identified. Without that full sequence, we cannot agree with Appellants that they were possession of the claimed nucleic acid sequences. In Amgen v. Chugai, we explained that:

> A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical com-

> pound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, . . . because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

927 F.2d at 1206. Until Appellants obtained the complete amino acid sequence of TBP-II, they had no more than a wish to know the identity of the DNA encoding [**13] it.

As Appellants point out, we have recognized that the written description requirement can in some cases be satisfied by functional description. See, e.g., *Enzo, 296 F.3d at 1324* ("It is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement."). Nonetheless, such functional description can be sufficient only if there is also a structure-function relationship known to those of ordinary skill in the art. As we explained above, such a well-known relationship exists between a nucleic acid molecule's structure and its function in encoding a particular amino acid sequence: Given the amino acid sequence, one can determine the chemical structure of all nucleic acid molecules that can serve the function of encoding that sequence. Without that sequence, however, or with only a partial sequence, those structures cannot be determined and the written description requirement is consequently not met. As we explained in Enzo, the Guidelines for Examination of Patent Applications under the *35 U.S.C. § 112, P 1, "Written Description" Requirement, 66 Fed. Reg. 1099* [**14] *(Jan. 5, 2001)* ("Guidelines"), state that

> the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Guidelines, 66 Fed. Reg. at 1106* (emphasis added).

Enzo, 296 F.3d at 1324-25 (emphasis added). Appellants have provided no evidence that there is any known or disclosed correlation between the combination of a partial structure of a protein, the protein's biological activity, and the protein's molecular weight, on the one hand, and the structure of the DNA encoding the protein on the other.

CONCLUSION

The Board correctly affirmed the examiner's determination that the specification of the '129 application does not provide an adequate written description of the pending [*1336] claims. Accordingly, the Board's decision is

AFFIRMED.